

Editorial



Circular RNAs: New Therapeutic Targets for Cardiovascular Diseases

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► See the article “CircZNF609 Aggravated Myocardial Ischemia Reperfusion Injury via Mediation of miR-214-3p/PTGS2 Axis” in volume 52 on page 680.

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Circular RNAs (circRNAs) are known as non-coding RNAs covalently closed loop structures driven by back-splicing circularization.¹⁾ Although they were first identified in the early 1970s, their biological roles have been poorly studied due to the limited available technology. Recent advances in RNA sequencing technologies and bioinformatic tools prove that circRNAs are widely expressed in eukaryotic tissues and cells as a general feature of the human transcriptome.²⁾ CircRNAs have been considered as diagnostic biomarkers and therapeutic targets, because they exhibit tissue- or cell type-specific expression and are highly stable with a longer half-life and more resistant to digestion by exonucleases than linear RNAs.³⁾ Although the functions of most circRNAs are unknown, they can extensively bind miRNAs in the cytoplasm and function as miRNA sponges, which may regulate gene expression of their target mRNAs.⁴⁾ Some circRNAs largely accumulate in the nucleus and control their parent gene transcription. They may function as scaffolds for the assembly of macromolecular complexes as well as translating themselves to proteins in a cap-independent manner.⁵⁾

CircRNAs are also abundant in the human heart, and many studies have reported that they are involved in the regulation of the physiology and pathology of the cardiovascular system.^{6,7)} In a recent paper by Tang et al.⁸⁾ published in *Korean Circulation Journal*, the authors investigated the function of circZNF609 in in vitro and in vivo myocardial ischemia/reperfusion (I/R) injury models. CircZNF609 was upregulated in hypoxia/reoxygenation (H/R) model and its inhibition alleviated H/R induced apoptosis, reactive oxygen species generation, restored cell proliferation in cardiomyocytes and human umbilical vein endothelial cells. Furthermore, knockdown of circZNF609 significantly reduced the area of myocardial infarction and decreased myocardial cell apoptosis. Mechanically, circZNF609 directly sponged miR-214-3p and upregulated the expression of prostaglandin-endoperoxide synthase 2 (PTGS2). It is also known as cyclooxygenase 2 and is the key enzyme in the conversion of arachidonic acid to prostaglandin H₂, which is an important precursor of many other biologically significant molecules including prostacyclin and thromboxane A₂.⁹⁾ These findings support that circZNF609 can aggravate myocardial I/R injury by the activation of proinflammatory responses via mediation of miR-214-3p/PTGS2 axis.⁸⁾ However, in another relevant aspect of circZNF609, Legnini et al.¹⁰⁾ demonstrated that circZNF609 could be translated into a zinc-finger protein 609 in a splicing-dependent and cap-independent manner, and

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

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control myoblast proliferation in myogenesis. Therefore, further evaluation is required in order to elucidate the regulatory networks of circZNF609 involved in the pathogenesis of cardiovascular diseases.

Nowadays, the scientific interest is increasing in the field of circRNA research by breaking through the technological bottleneck for their comprehensive exploration. Although our knowledge is still insufficient to understand underlying mechanisms and functions of many circulating circRNAs, this research effort can make it possible to achieve a more accurate diagnosis and treatment strategy for cardiovascular diseases.

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